Insulin icodec-abae is approved by the US FDA for the treatment of T2D. It is not currently approved for the treatment of T1D, and its safety and efficacy have not been established for the treatment of T1D. There is no guarantee that insulin icodec-abae will be commercially available for the use(s) under investigation.

ONWARDS 1

Insulin-Naïve Adults with Type 2 Diabetes

Insulin Icodec-abae 700 units/mL injection vs **Insulin glargine injection, U-100**

Study Design

ONWARDS 1 was a Phase 3a, 78-week (52-week main phase and 26-week extension phase), randomized, open-label, treat-to-target trial comparing the safety and efficacy of once-weekly insulin icodec-abae to insulin glargine injection, U-100, Sanofi-Aventis U.S. LLC in insulin-naïve adult patients (≥ 18 years old) with type 2 diabetes and an A1C of 7-11%.[1]

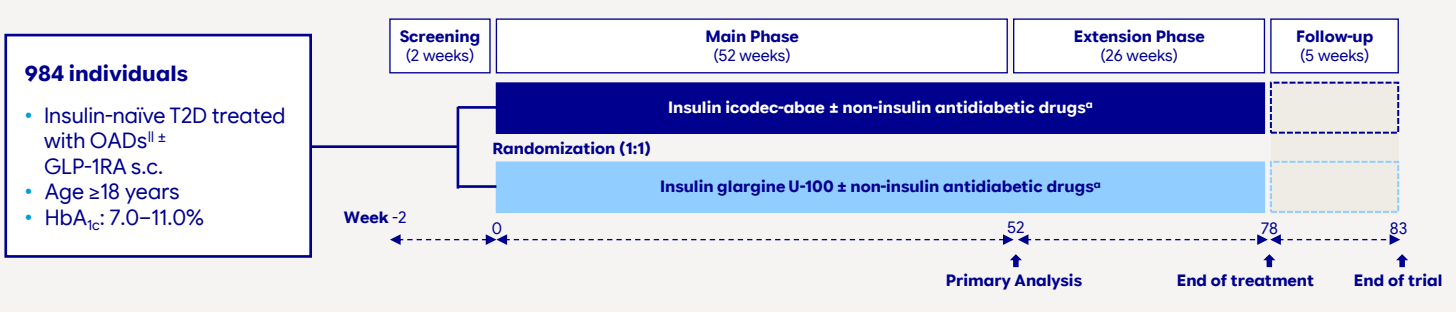
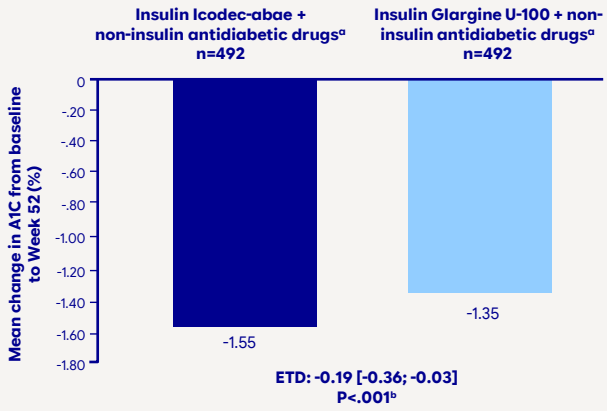


Figure 1. ONWARDS 1 Trial Design[1]

Primary Efficacy Endpoint

The primary endpoint was change in glycosylated hemoglobin (A1C) from baseline to Week 52.[1]



Secondary Efficacy Endpoints

Proportion of Time in Range (TIR) (%) from Week 48 to 52[c,d]

71.90% Insulin Icodec-abae — **66.90%** Insulin Glargine U-100

ETD: 4.27 [1.92; 6.62]
P<.001*

Proportion of Time Below Range (TBR) (%) from Week 48 to 52[c,d,**]

0.3% Insulin Icodec-abae — **0.20%** Insulin Glargine U-100

ETD: 1.27 [0.94; 1.71]
P=0.11

Patients achieving A1C <7% at Week 52 (%)

57.60% Insulin Icodec-abae — **45.40%** Insulin Glargine U-100

EOR: 1.63 [1.24; 2.14]

Safety

Combined level 2 or level 3 hypoglycemia from baseline to Week 52

	n (%)	E (rate per PYE)
Insulin Icodec-abae	**48 (9.8)**	**144 (0.30)**
Insulin Glargine U-100	52 (10.6)	78 (0.16)

ERR: 1.64 [0.98; 2.75]

Patients achieving A1C <7% at Week 52 without level 2 or 3 hypoglycemia (%)

52.60% Insulin Icodec-abae — **42.60%** Insulin Glargine U-100

1.49 [1.15; 1.94]

a. Most common background non-insulin glucose-lowering drugs included metformin, sulfonylureas, sodium-glucose cotransporter-2 (SGLT-2) inhibitors, glucagon-like peptide-1 (GLP-1) receptor agonists, and dipeptidyl peptidase-4 (DPP-4) inhibitors.
b. P-value for non-inferiority. Based on achievement of non-inferiority, superiority was then evaluated and confirmed (P=.02).
c. Measurements conducted via double-blinded continuous glucose monitoring (CGM) using the Dexcom G6 system.
d. Pre-specified secondary confirmatory endpoint.
*Statistically significant difference in favor of icodec-abae. **The percentage of time spent with glucose levels in the very low range (<54 mg/dL). ‖Pre-trial all OADs including oral GLP-1RAs are allowed but sulfonylureas and glinides are to be discontinued at randomization.
Abbreviations: A1C: glycosylated hemoglobin; E: episodes; EOR: estimated odds ratio; ERR: estimated rate ratio; ETD: estimated treatment difference; FPG: fasting plasma glucose; n: number of patients; PYE: Patient Year of Exposure.

1. Rosenstock J, et al. N Engl J Med. 2023;389(4):297-308.